

63-4-1

AAL-TDR-62-14

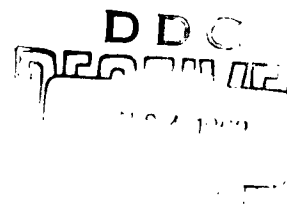
CATALOGED BY DDC

AS NO. 407391

SEPTAL AND HYPOTHALAMIC STIMULATION  
OF UNANESTHETIZED CATS

TECHNICAL DOCUMENTARY REPORT AAL-TDR-62-14

September 1962



ARCTIC AEROMEDICAL LABORATORY  
AEROSPACE MEDICAL DIVISION  
AIR FORCE SYSTEMS COMMAND  
FORT WAINWRIGHT, ALASKA

407 391

Project 8238-22

(Prepared under Contract AF41(657)-344 by  
D. G. Stuart, Y. Kawamura and A. Hemingway  
Department of Physiology, School of Medicine,  
University of California at Los Angeles)

## NOTICES

When US Government drawings, specifications, or other data are used for any purpose other than a definitely related government procurement operation, the government thereby incurs no responsibility nor any obligation whatsoever; and the fact that the government may have formulated, furnished, or in any way supplied the said drawings, specifications, or other data is not to be regarded by implication or otherwise, as in any manner licensing the holder or any other person or corporation, or conveying any rights or permission to manufacture, use or sell any patented invention that may in any way be related thereto.

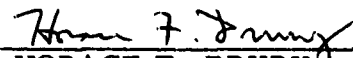
US Government agencies and other qualified ASTIA users may obtain copies of this report from the Armed Services Technical Information Agency, Documents Service Center, Arlington 12, Virginia.

This report has been released to the Office of Technical Services, U. S. Department of Commerce, Washington 25, D. C. , for sale to the general public.

## ABSTRACT

In six cats bipolar stainless steel electrodes were stereotactically implanted in septal and hypothalamic loci. Observations were made of autonomic, somatomotor and behavioral responses to electrical stimulation delivered while the cats were unanesthetized and unrestrained. Septal stimulation evoked sympathetic and parasympathetic responses in varying combinations on various days. This suggested that responses to septal stimulation were influenced by the relative excitability of anterior and posterior hypothalamic neurons at a given time. Shivering was produced during stimulation of both septal and hypothalamic loci, thereby confirming previous results obtained from anesthetized preparations.

## PUBLICATION REVIEW

  
\_\_\_\_\_  
HORACE F. DRURY  
Director of Research

# SEPTAL AND HYPOTHALAMIC STIMULATION OF UNANESTHETIZED CATS\*

## SECTION 1. INTRODUCTION

We have recently reported the consistent production of shivering in anesthetized cats during electrical stimulation of the dorso-medial region of the posterior hypothalamus (Stuart, 1961; Stuart et al, 1960). Less vigorous shivering, with a greater latency of onset, was produced during stimulation of the lateral septal region of the forebrain. When stimulating anesthetized cats to suppress shivering, a greater stimulus intensity was necessary for the medial septum than for the dorso-lateral boundary of the anterior hypothalamus and preoptic region, an area shown by others (Magoun et al, 1938; Hemingway et al, 1940; Andersson et al, 1956) to integrate heat loss mechanisms. Cold-induced shivering was abolished, or markedly reduced, in unanesthetized cats with lesions in the dorso-medial posterior hypothalamus. However, shivering was of normal intensity in cats with septal lesions.

The above observations suggested that septal influences on the efferent (motor) aspect of shivering were secondary to hypothalamic influences. This conclusion was based on stimulation experiments in which animals were lightly anesthetized with alpha chloralose or, in some cases, pentobarbital sodium. Reflexes tend to be hyperactive during light alpha chloralose anesthesia, and pentobarbital sodium, in light doses, may potentiate the shivering mechanism since animals may display shivering at normal body temperature in the waning stages of such anesthesia (Stuart, 1961). It thus seemed advisable to repeat our observations in unanesthetized and unrestrained animals.

This is a report of preliminary results on effects of septal and hypothalamic stimulation of unanesthetized cats.

## SECTION 2. METHODS

In six cats electrodes were stereotactically implanted in septal and hypothalamic loci to permit observation and recording in the unanesthetized and unrestrained state.

---

\* Submitted for publication August 1961.

Each preparation was first anesthetized (pentobarbital sodium, 33 mg/kg), its head mounted in the stereotaxic frame, scalp skin incised and reflected, temporal muscles retracted, and calvarium exposed. Bipolar stimulating electrodes similar to those described elsewhere (Stuart, 1961) were stereotactically placed at various subcortical sites by drilling appropriate holes in the calvarium. The electrodes were so designed that their tops protruded but 1 mm from the calvarium. The electrodes were permanently fixed by a cement (NuWeld, L. D. Caulk Co.) to the calvarium, the lead-off electrode wires being soldered to a female plug (Winchester Electronic Inc. Monobloc M 95), also cement attached to the skull. Various muscles of the fore- and hindlimbs were implanted with electrodes. The lead-off wires from the muscles were soldered to the female plug via subcutaneous route. With this technique it was possible to implant a total of 8 bipolar brain and/or muscle electrodes. There were 4 electrodes and a ground electrode to each 9 pin receptacle plug (monobloc, M9P) which could be inserted into each female plug attached to the skull. The cables were so suspended that the animal could freely move within the confines of a Faraday cage. Electrical stimuli could be applied through any given electrode and recordings made from the other electrodes.

Terminally the animals were sacrificed, their brains fixed in formalin, sectioned every 80  $\mu$ , and alternate sections stained with buffered thionine to permit localization of electrode tracts.

In Figures 1 through 5 the positions of the various electrodes in five of the cats are shown schematically. In such sketches each electrode is numbered and drawn to brain scale. At the bottom of each sketch of a frontal plane of the brain a second number appears that is a code for the particular stained section of nervous tissue on which the sketch is based. Table I is a key to abbreviations of nomenclature used in these figures.

### SECTION 3. RESULTS

The responses of these animals to electrical stimulation of various prosencephalic loci are listed in Tables II through VI. In these tables three columns of figures are listed under stimulus parameters. The first is stimulus intensity in  $\mu$ A/pulse, the second stimulus frequency in p/sec., and the third pulse duration in msec. Under responses are listed certain terms that embrace a variety of effects. In order of appearance they are:

Avoidance. This involved a backtracking of a few steps followed by an attempt to escape from the Faraday cage. The movements were not rapid nor accompanied by signs of anxiety or rage.

Purring. This was usually accompanied by pupillary constriction and assumption of a languid posture with weight supported on crouched hindlimbs, belly and flexed forelimbs. The eyes would close and the head slowly rock to the ground. In one case, denoted "postural relaxation," the above movements were not accompanied by purring.

Huddling. This posture involved an exaggeration of the above, except that the weight seemed distributed more to flexed limbs than to the belly. It was invariably accompanied by piloerection but not anxiety or rage.

Rage. This involved pupillary dilation, spitting, hissing, snarling, salivation, urination, piloerection, and rapidly executed nonspecific avoidance movements. In one instance, denoted "directed rage," the animal would leap directly at the investigator whose face fortunately was three inches outside the side wall of the cage.

Arousal. This involved pupillary dilation and assumption of an upright posture. The animal would make no avoidance movements but rather would direct his attention around the room.

Anxiety. This involved "arousal" coupled with what appeared to be a state of anxiety. It was not accompanied by "avoidance" or "rage."

Tremor. This involved alternating limb and neck flexor and extensor activity, resulting in a rocking motion. By palpation it could easily be distinguished from shivering in which the rate of tremor was faster, the amplitude of oscillation was less, and waxing and waning of muscle tone occurred synchronously in flexors and extensors.

In Figure 1 and Table II (cat no. IM. 1) the locus and response to stimulation of electrodes  $R^2$  and  $L^4$  are not listed because the former locus was in the dorsolateral anterior hypothalamus and the latter electrode was faulty with no stimulation possible. Additionally, the responses to stimulation through electrode  $L^2$  are not listed in Table II because the electrode was found to be in the prothalamus nucleus of the forebrain rather than the ventrolateral posterior septum at which structure it had been stereotactically aimed. In all cases stimulation through the electrode evoked rage. In this cat dorsolateral midseptal stimulation (electrode  $L^1$ ) consistently evoked urination, salivation, lacrimation, retching, together with piloerection and growling. Ventrolateral posterior septal stimulation (electrode  $R^1$ ) evoked avoidance 31 and 54 days after surgery but purring 104 days after surgery and huddling 108 days after surgery. Stimulation of a locus midway between the dorsomedial and ventromedial nuclei of the tuberal hypothalamus (electrode  $R^3$ ) evoked anxiety, huddling, piloerection and avoidance 16, 31, 54 and 108 days after surgery, respectively. Stimulation of the subthalamic nucleus (electrode  $L^3$ ) evoked huddling, piloerection and avoidance 31, 54

**TABLE I**

**Nomenclature: Key to Abbreviations**

|     |                           |     |                                |
|-----|---------------------------|-----|--------------------------------|
| AC  | commissura anterior       | OC  | chiasma opticum                |
| Acb | N. accumbens              | OT  | tractus opticus                |
| CC  | corpus callosum           | PC  | commissura posterior           |
| Cd  | N. caudatus               | Ped | Pedunculus cerebri             |
| CI  | capsula interna           | PO  | regio praeoptica               |
| CM  | N. centrum medianum       | Pul | Pulvinar                       |
| DBB | Diagonal band of Broca    | Put | Putanem                        |
| En  | N. entopeduncularis       | R   | N. Reticularis                 |
| Fcd | Fundis caudati            | Re  | N. reuniens                    |
| Fx  | fornix                    | S   | Stria medullaris               |
| GL  | geniculatum laterale      | Spt | area septalis                  |
| GP  | Globus pallidus           | Sn  | Substantia nigra               |
| LME | Lamina medullaris externa | Su  | N. subthalamicus               |
| MI  | massa intermedia          | TMT | tractus mamillo-thalamicus     |
| Mm  | corpus mamillare          | Vm  | N. ventralis postero-lateralis |
| NCM | N. centralis medialis     | VPM | N. ventralis postero-medialis  |
| NPr | N. prothalamicus          | Zi  | Zona incerta                   |

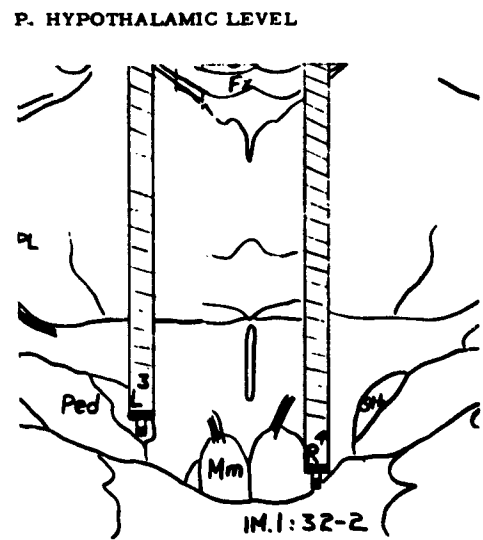
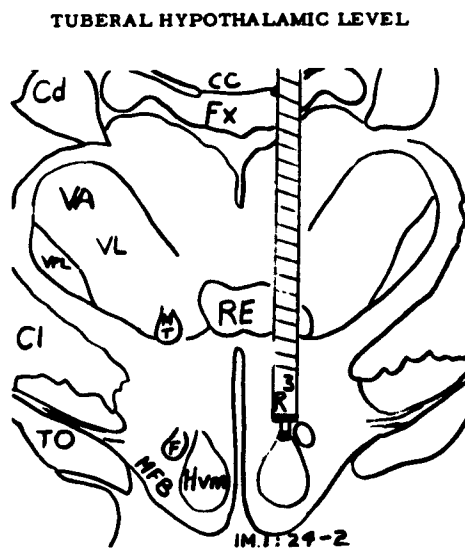
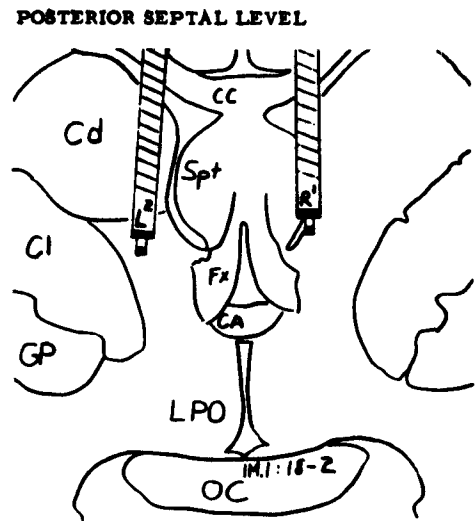
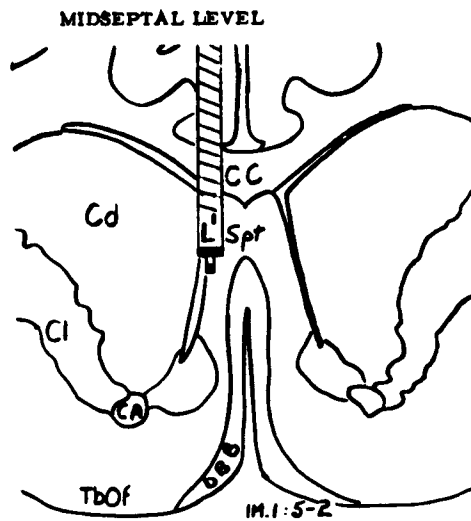


FIGURE 1

Schematic Frontal Representations of  
Electrode Tracts in Cat No. IM. 1.



**TABLE II**  
**RESPONSES OF UNANESTHETIZED CAT NO. IM. 1 TO ELECTRICAL**  
**STIMULATION OF VARIOUS PROSENCEPHALIC LOCI**

| Region   | Days<br>After<br>Surgery         | Stimulus<br>Parameters  | Responses   |
|--|----------------------------------|---|---|
| Midseptum<br>(Dorsolateral)<br>Electrode L <sup>1</sup>              | 16<br>31<br><br>54<br>104<br>108 | 500-50-1<br>1600-100-1<br>1600-100-3<br>1600-100-1<br>800-25-1<br>800-25-1    | Growling, avoid., urination<br>Avoidance, urination<br>Salivation, lacrim., urin.<br>Pilo., urin., retching<br>Grow., saliv., urin., pilo<br>Piloerection |
| Post. Septum<br>(Ventrolateral)<br>Electrode R <sup>1</sup>          | 16<br>31<br>54<br>104<br>108     | 1600-100-1<br>1600-100-1<br>1600-100-1<br>1600-25-1<br>1600-100-1<br>800-25-1 | Anxiety<br>Avoidance<br>Avoidance<br>Purring<br>Purring<br>Huddling   |
| Subthalamic<br>Nucleus<br><br>Electrode L <sup>3</sup>               | 16<br>31<br>54<br>104<br>108     | 800-100-1<br>800-100-1<br>800-100-1<br>600-25-1<br>400-25-1                   | No response<br>Huddling<br>Piloerection<br>Avoidance<br>No response   |
| Tub.<br>Hypothalamus<br>(Dorsal)<br>Electrode R <sup>3</sup>         | 16<br>31<br>54<br>104<br>108     | 800-50-1<br>1600-50-1<br>800-25-1<br>800-25-1<br>800-25-1                     | Anxiety<br>Huddling<br>Piloerection<br>Avoidance<br>No response   |
| Post.<br>Hypothalamus<br>(Ventrolateral)<br>Electrode R <sup>4</sup> | 16<br>31<br>54<br>104<br>108     | 800-25-1<br>800-25-1<br>800-25-1<br>800-25-1<br>800-25-1                      | Purring<br>Purring<br>Purring<br>Purring<br>Purring   |

and 104 days after surgery, respectively. Stimulation of the ventrolateral, posterior hypothalamus (electrode R<sup>4</sup>) evoked purring. No shivering or tremor was seen in this cat.

In summary, for cat no. IM. 1 consistent sympathetic and parasympathetic responses were evoked by midseptal stimulation, but posterior septal, subthalamic and tuberal hypothalamic stimulation evoked on the same day an aroused state (avoidance) and on others a relaxed state (purring and huddling). However, on the same day all listed responses were repeatable.

Figure 2 and Table III list the loci and the responses to their stimulation in cat no. IM. 2. Stimulation of a dorsal midseptal locus (electrode L<sup>1</sup>) evoked copious urination 36 days after surgery but not 89 days after surgery, when arousal was evident. The shivering that was evoked 86 days after surgery was maintained for the duration of the stimulation but the latency involved was unknown since it was not the practice of the investigator to palpate the animal on the first trial stimulation. This response could not be repeated on subsequent trials. Stimulation of a contralateral midseptal site about 0.5 mm more lateral (electrode R<sup>1</sup>) did not evoke shivering or urination but rather piloerection and respiration rate increase, arousal, and growling 21, 36 and 86 days after surgery. Stimulation of a dorsal tuberal locus (electrode L<sup>2</sup>) in the immediate vicinity of the mammillothalamic tract evoked arousal and shivering 21 and 36 days after surgery, respectively. The latter response was replaced by rage when the intensity of stimulation was doubled. The shivering was reproducible but not without the response being replaced by avoidance in the course of stimulation. In this particular case shivering was only observed by independent observation and not by palpation. Stimulation of a contralateral hypothalamic site (electrode R<sup>2</sup>) about 1 mm caudal to electrode L<sup>2</sup> evoked shivering 21 days after surgery but this could not be repeated. Subsequently the responses were arousal and piloerection 36 and 86 days after surgery. Stimulation of a ventromedial posterior hypothalamic locus (electrode L<sup>3</sup>) evoked similar responses of anxiety and avoidance 21, 36 and 89 days after surgery. Stimulation of a contralateral locus about 1 mm more lateral (electrode R<sup>3</sup>) evoked a reproducible tremor that changed to rapid circling to the right when the stimulus intensity was increased.

In summary, for cat no IM. 2 shivering was seen while stimulating a midseptal, a tuberal and a posterior hypothalamic locus. On the same day in the former and latter loci it was not repeatable but in the case of the tuberal locus it was. In no case was the response seen on subsequent days. Again sympathetic and parasympathetic responses varied from day to day when stimulating a given locus but in no case was a directly opposite effect seen to that evoked on a preceding day.

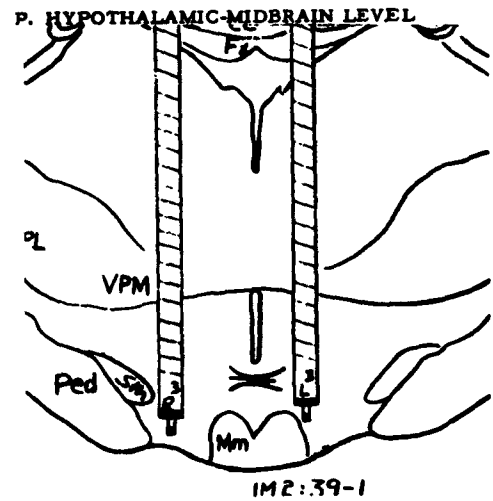
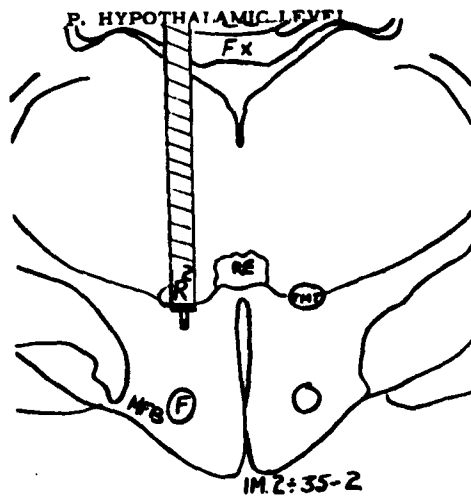
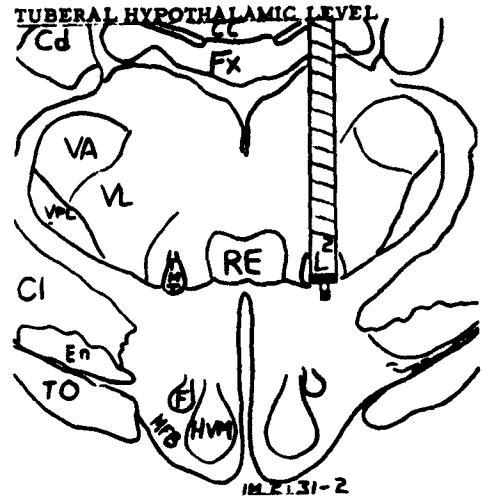
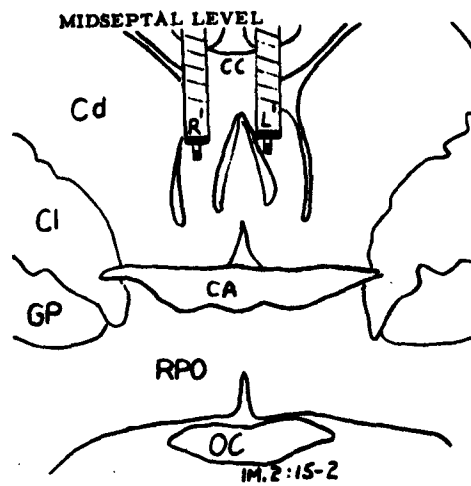


FIGURE 2

Schematic Frontal Representations of  
Electrode Tracts in Cat No. IM. 2.

TABLE III

RESPONSES OF UNANESTHETIZED CAT NO. IM. 2 TO ELECTRICAL  
STIMULATION OF VARIOUS PROSENCEPHALIC LOCI

| Region          | Days<br>After<br>Surgery | Stimulus<br>Parameters | Responses                 |
|-----------------|--------------------------|------------------------|---------------------------|
| Midseptum       | 21                       | 1600-100-1             | Arousal                   |
| (Dorsal)        | 36                       | 1600-100-1             | Copious urination         |
| Electrode       | 86                       | 800-25-1               | Shivering                 |
| L <sup>1</sup>  | 89                       | 800-25-1               | Arousal                   |
|                 |                          | 800-25-1               | Same                      |
| Midseptum       | 21                       | 1600-100-1             | Resp. incr., piloerection |
| (Dorsolateral)  | 36                       | 1600-100-1             | Piloerection, arousal     |
| Electrode       | 86                       | 400-25-1               | Growling                  |
| R <sup>1</sup>  | 89                       | 800-25-1               | No response               |
| Tub.            | 21                       | 1600-100-1             | Arousal                   |
| Hypothalamus    | 36                       | 800-100-1              | Shivering                 |
| (Dorsal)        |                          | 1600-100-1             | Rage                      |
| Electrode       | 86                       | 400-25-1               | No response               |
| L <sup>2</sup>  | 89                       | 400-25-1               | No response               |
| Post.           | 21                       | 800-25-1               | Shivering                 |
| Hypothalamus    | 36                       | 800-100-1              | Arousal                   |
| Electrode       | 86                       | 1600-100-1             | Piloerection              |
| R <sup>2</sup>  | 89                       | 400-25-1               | No response               |
| Post.           | 21                       | 1600-100-1             | Anxiety                   |
| Hypothalamus    | 36                       | 400-100-1              | Piloerection              |
| (Ventromedial)  |                          | 800-100-1              | Extreme avoidance         |
| Electrode       | 86                       | 400-25-1               | No response               |
| L <sup>3</sup>  | 89                       | 800-25-1               | Avoidance, piloerection   |
| Post. Hypothal. | 21                       | 1600-100-1             | Tremor                    |
| (Ventrolateral) | 36                       | 600-100-1              | Tremor                    |
| Electrode       |                          | 1600-100-1             | Circling to right         |
| R <sup>3</sup>  | 86                       | 400-25-1               | No response               |
|                 | 89                       | 800-25-1               | No response               |

Figure 3 and Table IV list the loci and responses evoked by stimulation in cat no. IM. 3. Stimulation of a ventromedial midseptal locus (electrode L<sup>1</sup>) evoked shivering and piloerection 7 days after surgery but only piloerection 22, 72 and 75 days after surgery. Stimulation of a ventrolateral posterior septal locus (electrode R<sup>1</sup>) evoked piloerection and urination 7 and 22 days after surgery and piloerection and an increase in muscle tone 72 and 75 days after surgery. Stimulation of a ventromedial tuberal hypothalamic locus (electrode L<sup>2</sup>) evoked directed rage 7, 22, 72 and 75 days after surgery. This locus was about 0.5 mm caudal to the center of the ventromedial hypothalamic nucleus. Less intense stimuli of 100  $\mu$ A/pulse evoked no response and it would thus appear that directed rage was the threshold response. However, stimulation of a contralateral locus about 1 mm more caudal (electrode R<sup>2</sup>) evoked anxiety and ataxic movements but no rage. Stimulation of a ventrolateral posterior hypothalamic locus (electrode R<sup>3</sup>) evoked a disruption of spontaneous movements involved in ear scratching. Upon receiving the stimulus the animal's forelimb slowly descended to the floor in tremulous fashion but then would rebound to the ear only to fall away again. The observation was repeated the same day and one subsequent day.

In summary, in cat no. IM. 3 shivering was observed during posterior septal stimulation but could not be evoked repeatedly. Responses from stimulation of other loci were relatively consistent.

Stimulation of cat no. IM. 4 evoked few vigorous responses. The animal had a low level inspiratory infection and a generally enfeebled condition from surgery until sacrificed. As shown in Figure 4 and Table V there was little difference between responses evoked by stimulation of ventrolateral and ventromedial midseptal loci (electrodes 1 and 2). Stimulation of the prothalamus of the forebrain (again a mistake of placement in that the electrode, No. 3, had been stereotactically aimed at the ventrolateral posterior septum) evoked pupillary constriction, salivation, piloerection and increase in respiratory rate. In cat no. IM. 1 stimulation of this nucleus evoked rage. Possibly the responses listed above are similar but attenuated by the animal's enfeebled condition. No detectible response was observed by stimulation of a ventromedial posterior hypothalamic locus (electrode 4) but stimulation of a contralateral locus (electrode 5) evoked pupillary dilatation, an increase in respiratory minute volume 7 and 13 days after surgery, piloerection and huddling 34 days after surgery.

Figure 5 and Table VI list the loci and responses to their stimulation in cat no. IM. 6. Stimulation of a ventromidseptal locus (electrode 1) evoked pupillary dilatation and an increase in muscle tone 3, 9, 31 and 51 days after surgery. Stimulation of a contralateral dorsal midseptal locus (electrode 2) evoked pupillary dilatation three days after surgery, shivering and piloerection 9 days after surgery, an increase in muscle tone 31 days after surgery, and pupillary constriction, lacrimation and piloerection 51 days after surgery. The shivering observed was not repeatable on the

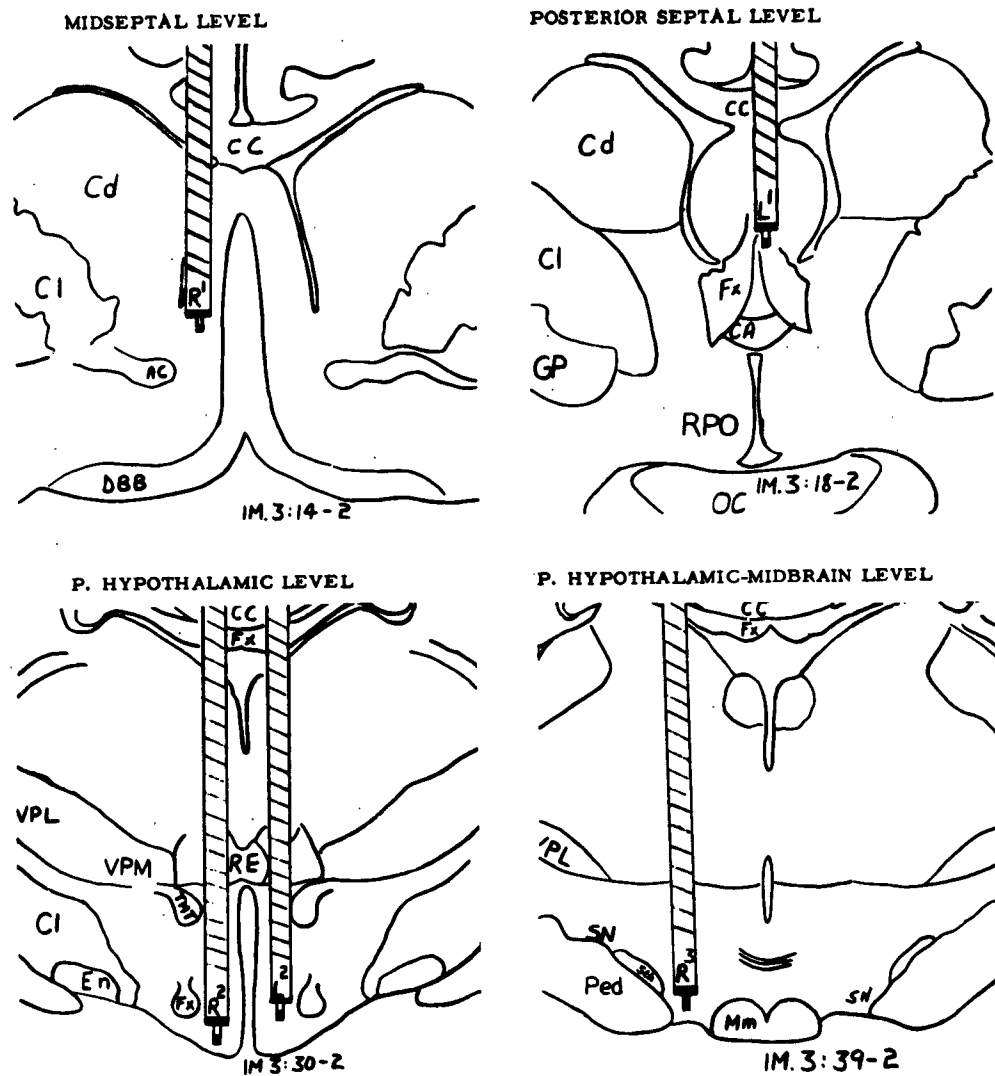


FIGURE 3

Schematic Frontal Representations of  
Electrode Tracts in Cat No. IM. 3.

TABLE IV

RESPONSES OF UNANESTHETIZED CAT NO. IM. 3 TO ELECTRICAL  
STIMULATION OF VARIOUS PROSENCEPHALIC LOCI

| Region                                   | Days<br>After<br>Surgery | Stimulus<br>Parameters | Responses  |
|--|--------------------------|------------------------|--|
| Post. Septum<br>(Ventromedial)           | 7                        | 800-100-1              | Shivering, piloerection                          |
|  | 22                       | 1600-100-1             | Piloerection                                     |
| Electrode                                | 72                       | 800-25-1               | Piloerection                                     |
| L <sup>1</sup>                           | 75                       | 800-25-1               | Piloerection                                     |
| Midseptum<br>(Ventrolateral)             | 7                        | 800-100-1              | Piloerection, urination                          |
|  | 22                       | 1600-100-1             | Piloerection, urination                          |
| Electrode                                | 72                       | 800-100-1              | Piloerection, m. tone incr.                      |
| R <sup>1</sup>                           | 75                       | 800-25-1               | Piloerection, m. tone incr.                      |
| Tub.<br>Hypothalamus<br>(Ventromedial)   | 7                        | 500-100-1              | Directed rage                                    |
|  | 22                       | 400-100-1              | No response                                      |
|  |                          | 500-100-1              | Directed rage                                    |
| Electrode                                | 72                       | 400-25-1               | No response                                      |
| L <sup>2</sup>                           |                          | 800-25-1               | Directed rage                                    |
|  | 75                       | 400-25-1               | Directed rage                                    |
| Tub.<br>Hypothalamus<br>(Ventromedial)   | 7                        | 500-100-1              | No response                                      |
|  | 22                       | 800-100-1              | No response                                      |
|  | 72                       | 800-25-1               | Anxiety  |
| Electrode                                | 75                       | 800-25-1               | Ataxic avoidance                                 |
| R <sup>2</sup>                           |                          |                        |  |
| Post.<br>Hypothalamus<br>(Ventrolateral) | 7                        | 400-25-1               | No response                                      |
|  | 22                       | 1600-100-1             | No response                                      |
|  | 72                       | 400-100-1              | Piloerection                                     |
| Electrode                                | 75                       | 400-25-1               | Disruption of spontaneous<br>locomotor movements |
| R <sup>3</sup>                           |                          |                        |  |

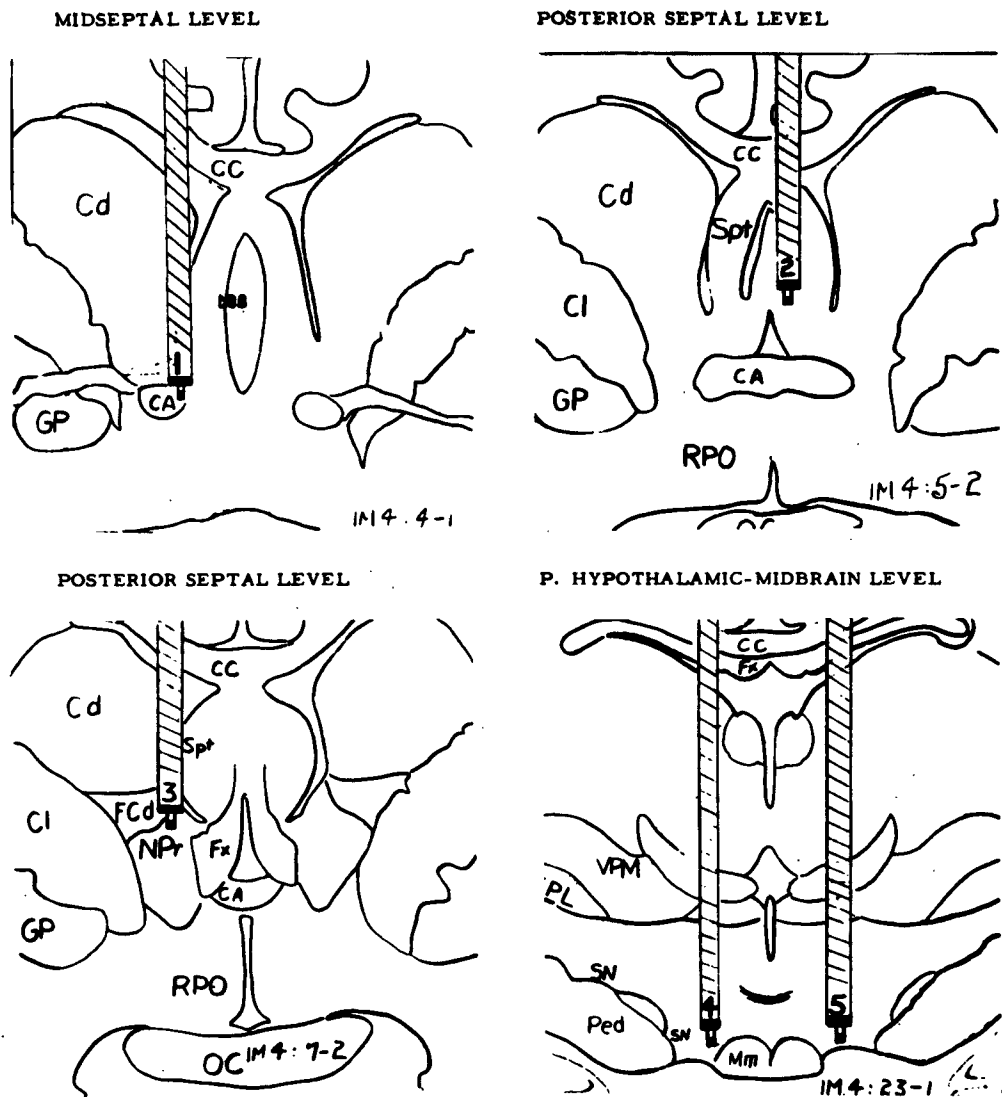


FIGURE 4

Schematic Frontal Representations of  
Electrode Tracts in Cat No. IM. 4.



**TABLE V**

**RESPONSES OF UNANESTHETIZED CAT NO. IM. 4 TO ELECTRICAL  
STIMULATION OF VARIOUS PROSENCEPHALIC LOCI**

| Region                       | Days<br>After<br>Surgery | Stimulus<br>Parameters | Responses                          |
|------------------------------|--------------------------|------------------------|------------------------------------|
| Midseptum<br>(Ventrolateral) | 7                        | 800-25-1               | Resp., inc., pupil. dilat.         |
|                              | 13                       | 800-25-1               | Pupil. dilat.                      |
| Electrode 1                  | 34                       | 800-25-1               | Resp. inc., pupil. dilat.          |
| Midseptum<br>(Ventromedial)  | 7                        | 800-25-1               | Arousal                            |
|                              | 13                       | 800-25-1               | Arousal                            |
| Electrode 2                  | 34                       | 800-25-1               | No response                        |
| Nuc.                         | 7                        | 800-25-1               | Pupil. constriction                |
| Prothalamicus                | 13                       | 800-25-1               | Saliv., pupil. const., resp. incr. |
| Electrode 3                  | 34                       | 800-25-1               | Piloerection                       |
| Post.                        | 7                        | 800-25-1               | No response                        |
| Hypothalamus                 | 13                       | 800-25-1               | No response                        |
| Electrode 4                  | 34                       | 800-25-1               | No response                        |
| Post.                        | 7                        | 800-25-1               | Resp. incr., pupil. dilat.         |
| Hypothalamus                 | 13                       | 800-25-1               | Resp. inc., pupil. dilat.          |
| Electrode 5                  | 34                       | 800-25-1               | Piloerection, huddling             |

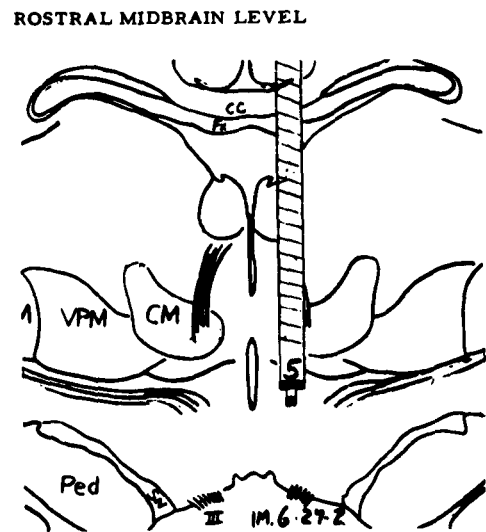
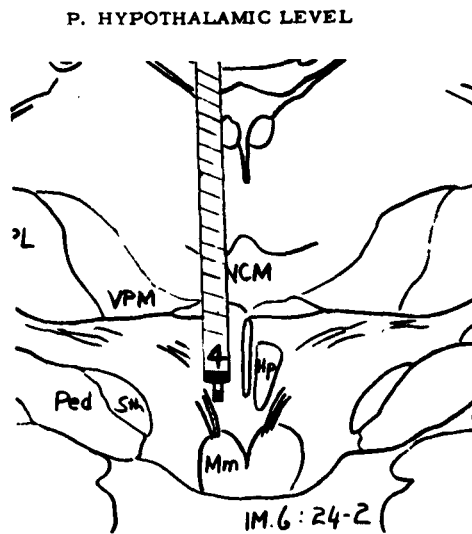
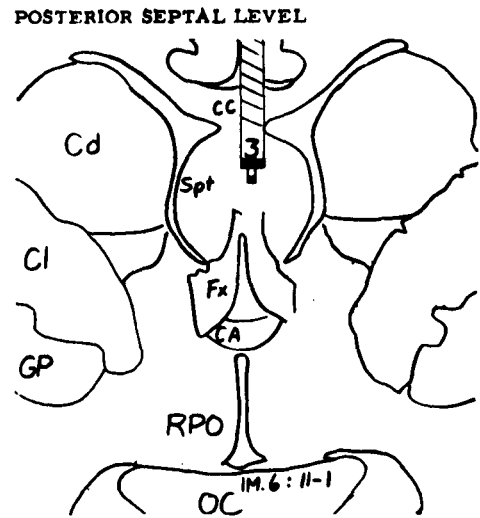
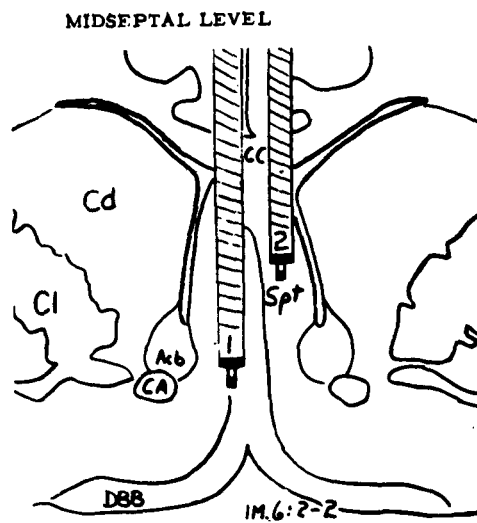


FIGURE 5

Schematic Frontal Representations of  
Electrode Tracts in Cat No. IM. 6.

TABLE VI

RESPONSES OF UNANESTHETIZED CAT NO. IM. 6 TO ELECTRICAL  
STIMULATION OF VARIOUS PROSENCEPHALIC LOCI

| Region                               | Days<br>After<br>Surgery | Stimulus<br>Parameters | Responses                         |
|--------------------------------------|--------------------------|------------------------|-----------------------------------|
| Midseptum<br>(Ventromedial)          | 3                        | 800-100-1              | Pupil. dilat., m. tone inc.       |
|                                      | 9                        | 800-25-1               | Pupil. dilat., m. tone inc.       |
|                                      | 31                       | 800-25-1               | Pupil. dilat., m. tone inc.       |
| Electrode 1                          | 51                       | 800-25-1               | Pupil. dilat., m. tone inc.       |
| Midseptum<br>(Dorsal)                | 3                        | 800-100-1              | Pupil dilat.                      |
|                                      | 9                        | 800-25-1               | Shivering                         |
|                                      | 31                       | 800-25-1               | M. tone increase                  |
| Electrode 2                          | 51                       | 800-25-1               | Pupil.constric.,lacrim.,piloerec. |
| Post. Septum<br>(Dorsomedial)        | 3                        | 800-100-1              | Lacrim., pupil. dilat.            |
|                                      | 9                        | 800-25-1               | Rage                              |
|                                      | 31                       | 800-25-1               | Rage                              |
| Electrode 3                          | 51                       | 800-25-1               | Rage                              |
| Post. Hypothal.<br>(Dorsomedial)     | 3                        | 800-100-1              | Pilo., m. tone inc.               |
|                                      | 9                        | 800-25-1               | Pilo., shivering                  |
|                                      | 31                       | 800-25-1               | Pilo., shivering                  |
| Electrode 4                          | 51                       | 800-25-1               | Pilo., resp. incr.                |
| Rostral<br>Midbrain<br>(Dorsomedial) | 3                        | 800-100-1              | Resp. incr., pilo.                |
|                                      | 9                        | 800-25-1               | Shivering, huddling               |
|                                      | 31                       | Not tested             |                                   |
| Electrode 5                          | 51                       | Not tested             |                                   |

same or any subsequent day. Stimulation of a dorsomedial posterior septal locus (electrode 3) evoked rage 9, 31, and 51 days after surgery. Stimulation of a dorsomedial posterior hypothalamic locus (electrode 4) evoked piloerection and an increase in muscle tone three days after surgery and piloerection and shivering 9 and 31 days after surgery. Stimulation of a dorsomedial midbrain locus (electrode 5) evoked shivering 9 days after surgery. The response was consistent on this day but not the previous day of stimulation.

#### SECTION 4. DISCUSSION

Such a variety of autonomic, somatomotor and behavioral effects, observed during stimulation of unanesthetized animals, is not obvious when stimulating anesthetized animals mounted in a stereotaxic frame. Additionally the use of unanesthetized animals unmasks the unphysiological nature of electrical stimulation. Thus this form of stimulation evokes hyperactivity in a small circumscribed region of the brain. In anesthetized animals this produces changes in heart rate, muscle tone, etc., but in unanesthetized animals, as well as evoking these same changes, results in bizarre behavior and somatomotor activity.

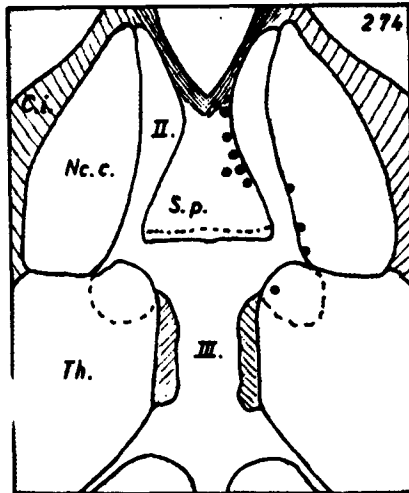
The various responses are listed in order to demonstrate that septal stimulation evoked both sympathetic and parasympathetic responses in varying combinations on various days. With attention focused mainly on somatomotor activity, it was difficult to make detailed observations of visceral responses. However, such varying responses support the concept that from any given region of the septum there are diffuse projections to both the anterior and posterior hypothalamus. Thus, activation of septal neurons can lead to predominantly sympathetic or parasympathetic responses, depending upon the relative excitability of anterior and posterior hypothalamic neurons at a given time.

These experiments have illustrated that shivering can be produced during stimulation of both septal and hypothalamic loci in unanesthetized cats. This confirms the results obtained from anesthetized preparations. The failure to reproduce shivering during repeated stimulation of the same septal locus is a result similar to that reported by Akert and Kesselring (1951). Their animals were stimulated at normal body temperature in a relatively warm environment (25° to 30° C). If their animals and those described above had been subjected to cooling during stimulation, shivering may have been more reproducible because Andersson (1957) found it was more easily produced during stimulation of unanesthetized goats when the animals were placed in a cold chamber.

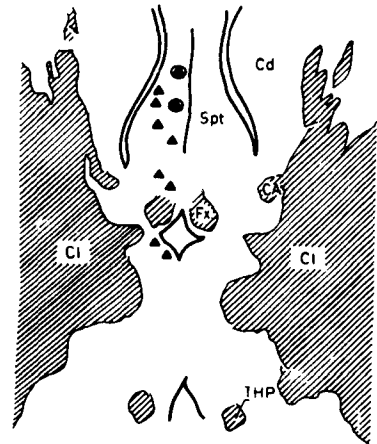
The discrepancy between our results and those of Akert and Kesselring and of Andersson concerning the localization of the septal regions stimulation of which evokes shivering is illustrated in Figure 6. "A" and "B" are schemata of cat and goat brain horizontal sections, illustrating that Akert and Kesselring found that such loci were lateral whereas Andersson, working with goats, found them more medial within the septum. "C" is a photograph of a frontal section through the brain of a cat from our study in which the electrode pierced the lateral portion of the septum. This was typical of all septal loci wherein stimulation evoked shivering. The goat has a septum proportionately larger than the cat's. As such, the anatomical organization of efferent projections may differ. Another explanation may be that Andersson used a stimulus that combined high frequency (50 p/sec.) with a long pulse (7 msec.) whereas Akert and Kesselring used a low frequency (5-15 p/sec.) with a long pulse (12 msec.). We used a high frequency (50-100 p/sec.) with a short pulse (1-3 msec.).

Stimulation of the septum has been found by the Ranson school (Ranson et al, 1935) to evoke cardiovascular and respiratory changes; by Hess (1957) to cause, in addition, urination, defecation and grooming; by Kurotsu (Kurotsu et al, 1958) to lead to suppression of gastric motility; by Harterius (1937) to cause ovulation; and by Olds (1958) to induce self-stimulation. To McLean (1959) the limbic system, of which the septum is an integral part, is concerned with self-preservation and preservation of the species. Thus most of the functions known to be influenced at the hypothalamic level are included. On the basis of our results it could be suggested that the septal role in mediating both facilitating and inhibiting influences on shivering is probably similar to its role in many other functions primarily controlled or influenced by the hypothalamus.

**A AKERT & KESSELRING**  
(Anesthetized Cats)



**B ANDERSSON**  
(Unanesthetized Goats)



**C. STUART, KAWAMURA & HEMINGWAY**  
(Anesthetized and Unanesthetized Cats)



**FIGURE 6**

The Production of Shivering by Septal Stimulation.

## REFERENCES

1. Akert, K. and F. Kesselring. Kaltezittern als Zentrale Reizeffect. *Helvet. physiol. et pharmacol. acta* 9:290, 1951.
2. Andersson, B. Cold defense reactions elicited by electrical stimulation within the septal area of the brain in goats. *Acta. physiol. scandinav.* 41:90, 1957.
3. Andersson, B., R. Grant and S. Larsson. Central control of heat loss mechanism in the goat. *Acta physiol. scandinav.* 37:261, 1956.
4. Harterius, H. O. Studies on a neurohypophyseal mechanism influencing gonadotropic activity. *Cold Spring Harbor Symp. Quant. Biol.* 5:280, 1937.
5. Hemingway, A., T. Rassmussen, H. Wickoff and A. T. Rassmussen. Effects of heating the hypothalamus of dogs by diathermy. *J. Neurophysiol.* 3:329, 1940.
6. Hess, W. R. The functional organization of the diencephalon. Grune and Stratton, New York, 1957.
7. Kurotsu, T., A. Sakai, A. Megawa and T. Ban. The changes in blood pressure and gastric motility induced by electrical stimulation of the preoptic and septal areas. *Med. J. of Osaka Univ.* 9:201, 1958.
8. Magoun, H. W., F. Harrison, J. R. Brobeck and S. Ranson. Activation of heat loss mechanisms by local heating of the brain. *J. Neurophysiol.* 1:101, 1938.
9. McLean, P. D. The limbic system with respect to two basic life principles. In *The Central Nervous System and Behavior. Trans. of 2nd Conf. Josiah Macy Jr. Found. Edited by M. A. B. Brazier.* New York, 1959.
10. Olds, J. Selective effects of drives and drugs on the "reward" system of the brain. p. 124 in *Neurological Basis of Behavior. Ciba Foundation Symposium. J. and A. Churchill Ltd., London, 1958.*
11. Ranson, S. W., H. Kabat and H. W. Magoun. Autonomic responses to electrical stimulation of hypothalamus preoptic region and septum. *Arch. of Neurol.* 33:467, 1935.

12. Stuart, D. G. Role of the prosencephalon in shivering. In Proceedings, Symposia on Arctic Biology and Medicine. I. Neural Aspects of Temperature Regulation. Arctic Aeromedical Laboratory, 1961.
13. Stuart, D. G., Y. Kawamura and A. Hemingway. Septal versus hypothalamic control of shivering. The physiologist 3(3):156, 1960



|  |   |
|--|---|
| <p>Arctic Aeromedical Laboratory, United States Air Force (AFSC), APO 731, Seattle, Wash.<br/>Rpt. AAL-TDR-62-14. SEPTAL AND HYPOTHALAMIC STIMULATION OF UNANESTHETIZED CATS. September 1962. 40 p. inc. tables, illus., 13 ref.</p> <p>Unclassified Report</p> <p>In six cats bipolar stainless steel electrodes were stereotactically implanted in septal and hypothalamic loci. Observations were made of autonomic, somatomotor and behavioral responses to electrical stimulation delivered while the cats were unanesthetized and unrestrained. Septal stimulation evoked sympathetic and parasympathetic responses in varying combinations on various days. This suggested that responses to septal stimulation were influenced by the relative excitability of anterior and posterior hypothalamic neurons at a given time. Shivering was produced during stimulation of both septal and</p> | <ol style="list-style-type: none"> <li>1. Hypothalamus</li> <li>2. Brain</li> <li>3. Shivering</li> <li>4. Cats</li> </ol> <ol style="list-style-type: none"> <li>I. Project 8238-22</li> <li>II. Contract AF41(657)-344</li> <li>III. Univ. of California at Los Angeles</li> <li>IV. Stuart, D. G., Y.</li> <li>V. Kawamura, A. Hemingway</li> <li>VI. Available from OTS</li> <li>VI. In ASTIA collection</li> </ol> |
| <p>hypothalamic loci, thereby confirming previous results obtained from anesthetized preparations.</p>   |   |

|  |   |
|--|---|
| <p>Arctic Aeromedical Laboratory, United States Air Force (AFSC), APO 731, Seattle, Wash.<br/>Rpt. AAL-TDR-62-14. SEPTAL AND HYPOTHALAMIC STIMULATION OF UNANESTHETIZED CATS. September 1962. 40 p. inc. tables, illus., 13 ref.</p> <p>Unclassified Report</p> <p>In six cats bipolar stainless steel electrodes were stereotactically implanted in septal and hypothalamic loci. Observations were made of autonomic, somatomotor and behavioral responses to electrical stimulation delivered while the cats were unanesthetized and unrestrained. Septal stimulation evoked sympathetic and parasympathetic responses in varying combinations on various days. This suggested that responses to septal stimulation were influenced by the relative excitability of anterior and posterior hypothalamic neurons at a given time. Shivering was produced during stimulation of both septal and</p> | <ol style="list-style-type: none"> <li>1. Hypothalamus</li> <li>2. Brain</li> <li>3. Shivering</li> <li>4. Cats</li> </ol> <ol style="list-style-type: none"> <li>I. Project 8238-22</li> <li>II. Contract AF41(657)-344</li> <li>III. Univ. of California at Los Angeles</li> <li>IV. Stuart, D. G., Y.</li> <li>V. Kawamura, A. Hemingway</li> <li>VI. Available from OTS</li> <li>VI. In ASTIA collection</li> </ol> |
| <p>hypothalamic loci, thereby confirming previous results obtained from anesthetized preparations.</p>   |   |